

Pregnancy outcomes and outdoor air pollution: an ecological study in districts of the Czech Republic 1986-8

Martin Bobak, David A Leon

Abstract

Objectives—Outdoor air pollution has consistently been shown to predict mortality. The finding that this association is stronger in infants than in children or adults raises the question whether air pollution could also be related to pregnancy outcomes—such as birthweight and stillbirth. The association between outdoor air pollution and stillbirths and low birthweight in the Czech Republic, where air pollution was high, was examined.

Methods—An ecological study was conducted, with routinely collected data on stillbirths and low birthweight (<2500 g), air pollution (total suspended particulates, sulphur dioxide (SO₂), and nitrogen oxides (NO_x)), and socioeconomic factors (mean income, car ownership, divorce rate, etc). The analyses were restricted to 45 districts on which data on air pollution were available for the period 1986-8. The effects of exposure variables on frequency of pregnancy outcomes were estimated by logistic regression with district-years as the units of analysis.

Results—Stillbirth rate (4.2/1000 births in monitored districts) was not significantly associated with any indicator of air pollution, and was weakly related to mean income and proportion of births outside marriage. Crude prevalence of low birthweight (prevalence 5.5%) showed highly significant associations with several socioeconomic factors; after controlling for these, odds ratios (ORs) / 50 µg/m³ increase in pollutant were: 1.04 (95% confidence interval (95% CI) 0.96 to 1.12) for total suspended particles, 1.10 (1.02 to 1.17) for SO₂, and 1.07 (0.98 to 1.16) for NO_x. When all pollutants were included in one model, SO₂ remained related to low birthweight (OR 1.10 (1.01 to 1.20), p=0.033).

Conclusion—These results are consistent with a recent study in China where birthweight was also associated with total suspended particles and SO₂ but ecological studies must be interpreted cautiously. Residual confounding by socioeconomic factors cannot be ruled out. The association between air pollution and birthweight requires further investigation.

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Keywords: air pollution; pregnancy; birthweight; stillbirth; socioeconomic factors; epidemiology

Ambient air pollution has been repeatedly shown to be strongly associated with mortality in both time series¹ and cross sectional studies,² with particulates being most consistently linked with adverse health effects.³ The finding of strong effects of air pollution in infancy⁴ raises the question whether pollution could also influence birthweight or other pregnancy outcomes.

Although such effects have been suspected,⁵ only a few published reports have examined this issue. A British study did not find an increased prevalence of low birthweight near a source of air pollution.⁶ By contrast, a recent study in Beijing, China, found that concentrations of particulates and sulphur dioxide (SO₂) during the third trimester of pregnancy were associated with birthweight, after controlling for season and individually measured covariates.⁷ Most recently, a careful comparison of two Czech districts found that exposure to high levels of air pollution in the first trimester of pregnancy were related to higher risk of low birthweight.^{11,12}

There are two main problems with accepting these associations as potentially causal. Firstly, it is not known how consistent is the association between air pollution and birthweight across different populations and datasets. Secondly, the biological mechanisms for such an association are not clear. In this report, we have considered the first issue. We have previously used data on air pollution and births collected routinely in districts of the Czech Republic in 1986-8 to study infant mortality.⁸ Prompted by the recent reports about birthweight, we have reanalysed these data to examine the possible association between air pollution and two pregnancy outcomes: low birthweight and stillbirths.

Methods

This ecological study analysed data from 45 of the 85 administrative districts of the Czech Republic where air pollution was monitored by the National Public Health Service 1986-8.⁹ Most districts had at least three monitoring stations, most of them were in the principle towns of the districts. The monitoring stations provided daily averages of total suspended particulates, sulphur dioxide (SO₂), and the sum of oxides of nitrogen (NO_x). Uniform methods of measurement were used in all districts: total suspended particles were measured by the gravimetric method, and SO₂ and NO_x by spectrophotometry. In the period covered by this study, public health services in the Czech

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The Effect of Air Pollution on Infant Mortality Appears Specific for Respiratory Causes in the Postneonatal Period

Martin Bobak¹ and David A. Leon²

To examine the association between individual lifetime measures of mean exposure to air pollution and postneonatal respiratory deaths, we have conducted a matched population-based case-control study covering all births registered in the Czech Republic from 1989 to 1991 that were linked to death records. For each case of infant death, we have randomly selected 20 controls from infants of the same sex born on the same day and alive when the case died. Exposure was assigned as the arithmetic mean of all 24-hour air pollution measurements in the district of residence of each case and control for the period between the birth and death of the index case. We used conditional logistic regression to estimate the effects of suspended particles, sulfur dioxide, and nitrogen oxides on risk of death in the neonatal and postneonatal period, controlling for maternal socioeconomic status and birth weight, birth length, and gestational age. There were 2,494 infant deaths

with exposure data on at least one pollutant, 133 of them from respiratory causes. The effects of all pollutants were strongest in the postneonatal period and were specific for respiratory causes. For these, rate ratios for a 50 $\mu\text{g}/\text{m}^3$ increase in particles, sulfur dioxide, and nitrogen oxides were 1.95 [95% confidence interval (CI) = 1.09–3.50], 1.74 (95% CI = 1.01–2.98), and 1.66 (95% CI = 0.98–2.81), respectively, after controlling for all covariates. Only particles showed a consistent association when all pollutants were entered in one model. We found no evidence of a relation between any pollutant and mortality from other causes. These results indicate that the effects of air pollution on infant mortality are specific for respiratory causes in the postneonatal period, are independent of socioeconomic factors, and are not mediated by birth weight or gestational age. (Epidemiology 1999;10:666–670)

Keywords: air pollution, infant mortality, respiratory disorders, age, particulate matter.

The effects of air pollution on mortality have been intensively studied since the London pollution episodes in the 1950s. There is now mounting evidence that the association may be causal, with particulate matter playing an important role.^{1–4} Although the mechanisms of the effects are not well understood, the strongest effects in adults have been seen for cardiorespiratory causes.^{2,3,5,6}

Time-series and geographic studies have suggested that the effects of air pollutants are particularly pronounced in children in the first year of life.^{7–10} We have previously reported that in an ecologic study in the Czech Republic the effects of air pollution on infant mortality appeared to be specific for respiratory causes in the postneonatal period.¹¹ This finding has been sup-

ported by the results of a larger study in U.S. metropolitan areas.¹²

The previous Czech study¹¹ was limited by the fact that the potential confounding by socioeconomic factors could only be controlled at the ecologic level. The U.S. study¹² had socioeconomic data at the individual level but did not assess the specificity of the effects for the postneonatal period, as it did not include neonatal deaths. This is an important issue, because these findings, if confirmed, can shed new light on the mechanisms of the effects and help to identify the susceptible population among infants; they can also provide perspective on the scale of the problem for determining appropriate public health measures.¹³ We have conducted a population-based case-control study with individual-level information on socioeconomic status and birth characteristics and with measures of cumulative lifetime exposure to pollutants specific for each individual. This study is based on years and subjects other than those examined in the previous Czech study.¹¹

Subjects and Methods

We have conducted a matched case-control study based on all singleton livebirths registered in the Czech Republic in 1989–1991. The national personal identity

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EDITORIALS

Air Pollution Kills Babies...

or so suggests a new study¹ from the Czech Republic, published in this issue of *Epidemiology*. This case-control study shows that exposure to air pollution was higher in infants who died when they were between 4 weeks and 12 months old than in control infants who survived. Using a unique set of registry data, the authors, Bobak and Leon, were able to adjust for various risk factors, including socioeconomic status, birth weight and length, and gestational age. The association was found to be specific for respiratory causes of death, which comprised about 13% of postneonatal infant deaths over all. The association was also stronger for particulate matter (PM, measured as total suspended particles, TSP) than for sulfur dioxide (SO₂) and nitrogen dioxide (NO₂), providing further evidence of the adverse health effects airborne particulate matter may have. Levels of exposure were relatively high in the study period (1989–1991), the 50th percentile of TSP being 68.7 $\mu\text{g}/\text{m}^3$.

The Czech study follows an earlier, less detailed report² that also found an association between postneonatal infant mortality and particulate matter air pollution. In the earlier study, potential confounders could not be controlled at the individual level, making the current study more convincing than the earlier one.

The issue of fatal effects of air pollution has received an enormous amount of attention in the last decade. The reason is that numerous time series studies have suggested that the day-to-day variation in air pollution concentrations is related to the day-to-day variation in the number of deaths in the population. There have also been some cohort studies suggesting that at low levels of exposure, PM exposure is associated with reduced survival.^{3,4} Neither the time series studies nor the cohort studies have paid much attention to deaths among the very young. In part, this is a problem of information: infant deaths are, fortunately, rare in the developed world, and one needs large populations studied over extensive periods of time to estimate effects on mortality in time series or cohort studies. It is, however, also a problem of where we focus our attention. Current dogma suggests that deaths related to air pollution as observed in time series studies occur primarily among the old and infirm, who may not have long to live anyway ("harvesting"). For this reason, it is sometimes even thought that the public health impact of air-pollution-related deaths is limited, when measured as reduced life expectancy. The cohort study findings clearly show that the effect on life expectancy could be substantial,⁵ and recent analyses of the harvesting issue

The Relationship between Selected Causes of Postneonatal Infant Mortality and Particulate Air Pollution in the United States

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Recent studies have found associations between particulate air pollution and total and adult mortality. The relationship between particulate air pollution and mortality among infants has not been examined in the United States. This study evaluates the relationship between postneonatal infant mortality and particulate matter in the United States. Our study involved analysis of cohorts consisting of approximately 4 million infants born between 1989 and 1991 in states that report relevant covariates; this included 86 metropolitan statistical areas (MSAs) in the United States. Data from the National Center for Health Statistics-linked birth/infant death records were combined at the MSA level with measurements of particulate matter 10 μm or less (PM_{10}) from the EPA's Aerometric Database. Infants were categorized as having high, medium, or low exposures based on tertiles of PM_{10} . Total and cause-specific postneonatal mortality rates were examined using logistic regression to control for demographic and environmental factors. Overall postneonatal mortality rates were 3.1 among infants with low PM_{10} exposures, 3.5 among infants with medium PM_{10} exposures, and 3.7 among highly exposed infants. After adjustment for other covariates, the odds ratio (OR) and 95% confidence intervals (CI) for total postneonatal mortality for the high exposure versus the low exposure group was 1.10 (1.04, 1.16). In normal birth weight infants, high PM_{10} exposure was associated with respiratory causes [OR = 1.40, (1.05, 1.85)] and sudden infant death syndrome [OR = 1.26, (1.14, 1.39)]. For low birth weight babies, high PM_{10} exposure was associated, but not significantly, with mortality from respiratory causes [OR = 1.18, (0.86, 1.61)]. This study suggests that particulate matter is associated with risk of postneonatal mortality. Continued attention should be paid to air quality to ensure optimal health of infants in the United States. **Key words:** air pollution, infant mortality, particulate air pollution, postneonatal mortality. *Environ Health Perspect* 105:608–612 (1997)

Concerns about the effects of particulate matter air pollution on health date back to the historic pollution episodes in London in 1952 when a weather inversion led to high levels of particulate matter air pollution and subsequent increases in mortality and morbidity (1). Since then, recent investigations of the relationship between air pollution and mortality in the United States have demonstrated an association between particulate air pollution levels and mortality at lower air pollution levels. A number of daily time-series studies have demonstrated an association between short-term exposure to particulate air pollution and mortality (2,3). More recent prospective cohort analyses have also demonstrated an association between long-term exposure to particulate air pollution and mortality (4,5). However, all the studies conducted in the United States have focused on adults. The original investigation in London observed increases in mortality for both adults over 45 years of age and children under the age of 1 year (1). Given this result and the number of studies showing a positive association between mortality and exposure to particulate air pollution in adults in the United States, it is reasonable to hypothesize a similar association might be observed in infants in the United States.

→ get these studies?

This hypothesis is supported by several factors. First, ecological studies in other countries have found an association between particulate air pollution and infant mortality (6–8); however, it is difficult to apply these results to the United States because particulate matter levels in these countries have typically been much higher than in the United States. Second, the results of previous studies among adults suggest vulnerable individuals, such as the elderly and people with preexisting cardiovascular or respiratory conditions, are more susceptible to effects from exposure to particulate air pollution than the rest of the population (9). Because of their high mortality rates, infants, particularly those born prematurely, may also fall into this group of susceptible individuals. Last, studies have found associations between particulate air pollution and respiratory illness in children (10,11).

Many studies of adults have examined the association of particulate air pollution with overall adult mortality as well as with specific causes of mortality (9,12). However, such an inclusive approach may not be appropriate for an analysis of air quality and mortality among infants. A majority of infant deaths are unlikely to be influenced by air pollution levels because

they occur too soon after birth (13) or are due to causes clearly intrinsic to the infant, such as congenital anomalies (14). To focus only on infant deaths that may plausibly be associated with particulate air pollution, we examined the relationship between exposure to particulate air pollution and selected causes of postneonatal mortality in the United States. Postneonatal death (death of an infant over 27 days of age) is thought to be influenced more by the infant's external environment than is mortality earlier in infancy (15). In keeping with the previously demonstrated relationship between particulate air pollution and childhood respiratory illness (10,11), an association between particulate air pollution and postneonatal mortality from respiratory causes can be postulated. Similarly, because several studies have suggested that sudden infant death syndrome (SIDS) is associated with exposure to environmental tobacco smoke (16,17), a potential association between SIDS and particulate air pollution is plausible.

Daily time-series analyses are commonly used to evaluate the relationship between short-term exposure to particulate air pollution and adult mortality. This method is not appropriate for an analysis of postneonatal mortality and pollution because of the small numbers of infants who die in a specific location over a short period of time. In adults, cohort analyses of specific cities or areas have been used to examine associations between mortality and chronic or long-term exposure to particulate matter. While this general approach may be feasible for a similar analysis among infants, geographically limited cohort analyses will also lack power due to small numbers.

The national-linked birth/infant death records provide a unique database for the examination of particulate air pollution and infant mortality. The birth certificate portion

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Subjects and Methods

We have conducted a matched case-control study based on all singleton livebirths registered in the Czech Republic in 1989–1991. The national personal identity

Air pollution and infant mortality in the Czech Republic, 1986-88

MARTIN BOBAK DAVID A. LEON

An ecological study of infant mortality and air pollution was conducted in the Czech Republic. Routinely collected data on infant mortality and air pollution in the period 1986-88 were analysed for the 46 of the 85 districts in the republic for which both were available. The independent effects of total suspended particulates (TSP-10), sulphur dioxide (SO₂), and oxides of nitrogen (NO_x) adjusted for district socioeconomic characteristics, such as income, car ownership, and abortion rate, were estimated by logistic regression.

We found weak positive associations between neonatal mortality and quintile of TSP-10 and SO₂. Stronger adjusted effects were seen for postneonatal mortality, with a consistent increase in risk from the lowest to the highest TSP-10 quintile ($p < 0.001$). Weaker and less consistent evidence of a positive association with NO_x ($p = 0.061$) was observed. The strongest effects were seen for postneonatal respiratory mortality, which increased consistently from lowest to highest TSP-10 quintile ($p = 0.013$). There was also a suggestion of a positive association with SO₂ ($p = 0.062$). The highest to lowest quintile risk ratios for postneonatal respiratory mortality were 2.41 (95% CI 1.10-5.28) for TSP-10, 3.91 (0.90-16.9) for SO₂, and 1.20 (0.37-3.91) NO_x.

The specificity of the association between air pollution quintile (especially TSP-10) and postneonatal respiratory mortality is consistent with the known effects of air pollution on respiratory disease morbidity in children. These ecological associations require confirmation in an individually based study.

Lancet 1992; 340: 1010-14.

Introduction

Czechoslovakia, especially the Czech Republic (the western and more industrialised of its two federal republics), has some of the highest levels of air pollution in Europe today. In 1987 it had the second highest annual emission of sulphur dioxide (22.4 tonnes/km²) in Europe.¹ It is estimated that more than 40% of sulphur pollution comes from neighbouring countries—mainly former East

Germany and Poland, less from West Germany and Austria.¹ The Czech Republic has varying terrain, including many hilly regions. Government estimates suggest that 60% of the population of the Czech Republic (total 10.4 million) live in highly polluted areas. Two-thirds of monitored districts in the Czech Republic recorded annual mean concentrations of suspended particulate matter in 1986-88 that were above World Health Organisation guidelines.²

Studies of the association between air pollution and health^{3,4} have tended not to look at infant mortality, despite the fact that it is plausible for infants to be especially vulnerable to air pollution. Those studies that have addressed this issue have reported positive correlations between air pollution and mortality in infancy from all causes⁵ or from respiratory disease⁶ or pneumonia.⁷ We have studied the strength of any association between air pollution within the Czech Republic and infant mortality, focusing on the extent to which different components of air pollution have independent effects upon mortality in the neonatal and postneonatal periods.

Data and methods

The study has an ecological design based on 46 of the 85 administrative districts of the Czech Republic subject to routine air pollution monitoring by the Czech Public Health Service in 1986-88. Most districts had at least three fixed monitoring stations, most of which were in the principal towns of the districts. These provided daily measurements throughout the year of concentrations of total suspended particulates up to 10 µm in size (TSP-10), sulphur dioxide (SO₂), and oxides of nitrogen (NO_x [NO plus NO₂]). The annual level of pollution in each district was defined as the geometric mean of all measurements taken within the district for that year, there being no seasonal pattern in the small number of days for which data were not available due to equipment failure. Atmospheric concentrations were measured by standard and uniform monitoring technology, TSP-10 by gravimetry, and SO₂ and NO_x by spectrophotometry.

The unit of analysis was the annual experience of each district, 5 of which were excluded because they did not have complete data for

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The Impact of Polycyclic Aromatic Hydrocarbons and Fine Particles on Pregnancy Outcome

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The relationship between intrauterine growth retardation (IUGR) and exposure to particulate matter $\leq 10 \mu\text{m}$ (PM_{10}) and particulate matter $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) in early pregnancy was recently studied in the highly polluted district of Teplice (Northern Bohemia). From this observation rose the question about the possible role of the carcinogenic fraction of polycyclic aromatic hydrocarbons (c-PAHs), which are usually bound to fine particles. The impact of c-PAHs and fine particles on IUGR was analyzed in Teplice and in Prachatic, a region with similarly high c-PAH but low particle levels. All European, single live births occurring in a 4-year period in Teplice ($n = 3,378$) and Prachatic ($n = 1,505$) were included. Detailed personal data were obtained via questionnaires and medical records. Mean PM_{10} , $\text{PM}_{2.5}$, and c-PAHs levels during the 9 gestational months (GM) were estimated for each mother. Adjusted odds ratios (AORs) of IUGR for three levels of c-PAHs (low, medium, and high) and for continuous data were estimated after adjustment for a range of covariates using logistic regression models. In the present 4-year sample from Teplice, previously published results about increasing IUGR risk after exposure to particles in the first GM were fully confirmed, but no such effects were found in Prachatic. The AOR of IUGR for fetuses from Teplice exposed to medium levels of c-PAHs in the first GM was 1.60 [confidence interval (CI), 1.06–2.15], and to high levels 2.15 (CI, 2.7–3.63). An exposure–response relationship was established by analyzing the continuous data. For each 10 ng increase of c-PAHs in the first GM, the AOR was 1.22 (CI, 1.07–1.39). About the same relationship was observed in Prachatic in spite of the low particle levels. The results prove that exposure to c-PAHs in early gestation may influence fetal growth. The particulate matter–IUGR association observed earlier may be at least partly explained by the presence of c-PAHs on particle surfaces. **Key words:** air pollution, fetal growth, intrauterine growth retardation, particulate matter, polycyclic aromatic hydrocarbons, reproductive effects. *Environ Health Perspect* 108:1159–1164 (2000). [Online 7 November 2000]

<http://ehpnet1.niehs.nih.gov/docs/2000/108p1159-1164dejmek/abstract.html>

There is widespread concern over the health effects of ambient air pollution (1,2). There is growing support for the idea that adverse pregnancy outcomes may result from maternal (parental) exposures to airborne pollution (3–8). A consistent relationship between maternal exposure to fine particles in early gestation and intrauterine growth retardation (IUGR) was recently observed in Teplice, a highly polluted district of northern Bohemia (9). One possible explanation for this finding is that rather than particles, some associated copollutant such as polycyclic aromatic hydrocarbons (PAHs) may interfere with fetal development. Most of these compounds are usually adsorbed on the surface of fine particles (10,11).

The genotoxicity and embryotoxicity of particulate matter in the ambient air of the Teplice district were also investigated (12). Extracts eluted from fine particles were examined by an *in vitro* acellular assay coupled with ³²P-postlabeling of DNA adducts and a chick embryotoxicity screening test. The extracts were able to preferentially produce DNA–PAH adducts in calf thymus DNA and were also embryotoxic. The highest

activity was found for fractions containing mainly PAHs (12). In addition, another study using the same population suggested that IUGR was positively related to the level of DNA–PAH adducts in placentae (13). These results indicate that PAHs are a major source of the genotoxic and embryotoxic activities of organic mixtures associated with the air pollution in the Teplice district.

This study examined the impact of PAHs on fetal growth in a larger data set from the same population. To enable a valid comparison, the effect of particulate matter on IUGR [examined recently in a 2-year data set (9)] was reanalyzed in this more complete (4-year) data set.

It is important to determine the real contribution (if any) of particulate matter and PAHs to the risk of IUGR; but this may not be an easy task. Dockery (14) discussed the methodologic problems in these types of studies: he suggested that such studies are intrinsically difficult because exposure is common, the expected effects are weak, the random misclassification of exposure is frequent, and the health indicators have multiple etiology. In addition, ambient air frequently represents

a complex mixture of pollutants (14). We attempted to overcome or minimize these problems by using a specific study design.

Exposure to ambient air pollution is common for populations living in a particular area. Because the heterogeneity of exposure is low, the distribution of possible health effects is hard to distinguish. In this respect, studies of the reproductive effects of common contaminants have a distinct advantage over studies of respiratory health effects or daily mortality. The probability of inducing some reproductive end points depends on the stage of the reproductive cycle (e.g., germinal mutations originate only before or during conception, and major birth defects invariably arise during the first 8 weeks of gestation). Thus, the induction of such effects is possible only in a relatively narrow sensitivity window. Some other reproductive outcomes may be less stage specific (e.g., spontaneous abortion, low birth weight). Air pollution levels vary considerably over the course of a year, whereas conceptions in the human population occur more or less continually. Therefore, it is possible to compare the prevalence of a particular stage-specific outcome in the offspring of parental groups that differ considerably in their exposure to certain pollutants during the same gestational stage.

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We are grateful to the many gynecologists and their staffs from the Departments of Obstetrics and Gynecology in the hospitals of Teplice, Duchcov, Prachatic, Vimperk, and Pisek. We thank them for their dedication and participation in this study. We also thank our colleagues from the District Institutes of Hygiene in Teplice and Prachatic for their support and collaboration.

This work was supported by grants from the Czech Ministry of Environment (Teplice Program II), the U.S. Environmental Protection Agency/U.S. Agency for International Development, and the Commission of European Communities (PHARE II, EC/HEA-18/CZ). This work is attributed to the Laboratory of Genetic Ecotoxicology, Regional Institute of Hygiene of Central Bohemia and Institute of Experimental Medicine, Academy of Sciences of the Czech Republic, Prague.

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LBW among term birth
 - 2.9% in Brno
 - 2.4% in Teplice
 - 2.3% in LA

Fetal Growth and Maternal Exposure to Particulate Matter during Pregnancy

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Prior studies reported an association between ambient air concentrations of total suspended particles and SO₂ during pregnancy and adverse pregnancy outcomes. We examined the possible impact of particulate matter up to 10 µm (PM₁₀) and up to 2.5 µm (PM_{2.5}) in size on intrauterine growth retardation (IUGR) risk in a highly polluted area of Northern Bohemia (Teplice District). The study group includes all singleton full-term births of European origin over a 2-year period in the Teplice District. Information on reproductive history, health, and lifestyle was obtained from maternal questionnaires. The mean concentrations of pollutants for each month of gestation were calculated using continuous monitoring data. Three intervals (low, medium, and high) were constructed for each pollutant (tertiles). Odds ratios (ORs) for IUGR for PM₁₀ and PM_{2.5} levels were generated using logistic regression for each month of gestation after adjustment for potential confounding factors. Adjusted ORs for IUGR related to ambient PM₁₀ levels in the first gestational month increased along the concentration intervals: medium 1.62 [95% confidence interval (CI), 1.07–2.46], high 2.64 (CI, 1.48–4.71). ORs for PM_{2.5} were 1.26 (CI, 0.81–1.95) and 2.11 (CI, 1.20–3.70), respectively. No other associations of IUGR risk with particulate matter were found. Influence of particles or other associated air pollutants on fetal growth in early gestation is one of several possible explanations of these results. Timing of this effect is compatible with a current hypothesis of IUGR pathogenesis. Seasonal factors, one of the other possible explanations, is less probable. More investigation is required to examine these findings and alternative explanations. **Key words:** air pollution, environmental exposure, fetal growth, intrauterine growth retardation, particulate matter, PM_{2.5}, PM₁₀, reproductive effects. *Environ Health Perspect* 107:475–480 (1999). [Online 4 May 1999]
<http://ehpnet1.niehs.nih.gov/docs/1999/107p475-480dejmek/abstract.html>

The Teplice Program, an international research project, was developed to evaluate health consequences of extremely elevated air pollution levels in Teplice, a district in the Northern Bohemia brown coal basin. Typically, air pollution in this area is composed of a high concentration of fine particles dominated by acid sulfates, polycyclic aromatic hydrocarbons (PAHs), nitrogen oxides, and toxic trace elements (1). The levels are especially high during meteorological inversions, which occur frequently during the fall and winter months. Changes in industry profiles, technological improvement of large power plants, and a rapid conversion of local heating systems from coal to gas, along with increasing traffic density, have resulted in changes in the pollutant levels and composition. With changes occurring after the political changes in the Czech Republic in 1989, a continual decrease of sulfur dioxide (SO₂) and particulate matter has been observed over the last several years. In the meantime, this area presented an opportunity to study the health effects while relatively high pollutant levels exist.

One of the major goals of the Teplice Program has been the possible effects of these pollutants on growth and development. To examine this, intrauterine growth retardation (IUGR) and measures of air pollution were examined.

Reduced fetal growth is one of the most important predictors of neonatal morbidity and mortality (2–4). Recent studies have also shown a relationship between some serious adult risks (namely noninsulin-dependent diabetes, hypertension, and coronary heart disease) and impaired growth in the prenatal and early postnatal period (5–7).

Preliminary analyses of the data collected during the first 18 months of the study resulted in two general observations: *a*) pollutant levels in this region (namely SO₂, particulate matter ≤ 10 µm in size (PM₁₀), and PAHs) were highest during the winter and lower in the summer, as measured by continuous air monitoring (8); and *b*) the prevalence of IUGR was greater for infants conceived during winter months than for those conceived in the summer (1). These preliminary observations are consistent with recent hypotheses for the etiology of IUGR—that initial changes leading to fetal growth retardation may be triggered in early pregnancy, around the time of implantation (9,10).

Other preliminary examinations of these data analyzed IUGR prevalence with selected air pollutants in early pregnancy. No association was observed for nitrogen oxides (NO_x). SO₂ and PM₁₀ levels in early pregnancy were significantly associated

with IUGR (11,12); the relationship of PM₁₀ to IUGR was confirmed in subsequent analyses in a more complete data set enlarged by additional 1996 data (12).

Particulate matter has been associated with acute cardio-respiratory morbidity and mortality in recent studies (13,14). Two common measures of particulate matter are PM₁₀ and particulate matter up to 2.5 µm in size (PM_{2.5}). The chemical composition of particles and of associated organics may vary by region, and is important to the understanding of potential toxicity (8).

The present study examines whether parental exposure to particulate matter in outdoor air during pregnancy is associated with IUGR. This evaluation uses ambient PM₁₀ and PM_{2.5} measurements to examine this issue.

Materials and Methods

The study group included all full-term singleton births of European origin in Teplice District from April 1994 through March 1996 to women with at least 1 year of residence in the district. All deliveries in Teplice District are hospitalized, allowing enrollment in the study during the hospital stay. The group was further restricted to the mother's first delivery during the study period. Preterm births (< 37 weeks gestation) were excluded from this analysis because of the

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Association between Air Pollution and Low Birth Weight: A Community-based Study

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The relationship between maternal exposure to air pollution during periods of pregnancy (entire and specific periods) and birth weight was investigated in a well-defined cohort. Between 1988 and 1991, all pregnant women living in four residential areas of Beijing were registered and followed from early pregnancy until delivery. Information on individual mothers and infants was collected. Daily air pollution data were obtained independently. The sample for analysis included 74,671 first-parity live births with gestational age 37–44 weeks. Multiple linear regression and logistic regression were used to estimate the effects of air pollution on birth weight and low birth weight (<2,500 g), adjusting for gestational age, residence, year of birth, maternal age, and infant gender. There was a significant exposure-response relationship between maternal exposures to sulfur dioxide (SO₂) and total suspended particles (TSP) during the third trimester of pregnancy and infant birth weight. The adjusted odds ratio for low birth weight was 1.11 (95% CI, 1.06–1.16) for each 100 µg/m³ increase in SO₂ and 1.10 (95% CI, 1.05–1.14) for each 100 µg/m³ increase in TSP. The estimated reduction in birth weight was 7.3 g and 6.9 g for each 100 µg/m³ increase in SO₂ and in TSP, respectively. The birth weight distribution of the high-exposure group was more skewed toward the left tail (i.e., with higher proportion of births <2,500 g) than that of the low-exposure group. Although the effects of other unmeasured risk factors cannot be excluded with certainty, our data suggest that TSP and SO₂, or a more complex pollution mixture associated with these pollutants, contribute to an excess risk of low birth weight in the Beijing population. **Key words:** air pollution, birth weight, low birth weight, sulfur dioxide (SO₂), total suspended particulates (TSP). *Environ Health Perspect* 105:514–520 (1997)

In both developed and developing countries, low birth weight is the most important predictor for neonatal mortality and is a significant determinant of postneonatal mortality and morbidity (1,2). Birth weight represents an endpoint of intrauterine growth, which depends on maternal, placental, and fetal factors, as well as a sequence of constitutional and environmental influences (3). An extensive list of risk factors for low birth weight has been reviewed (4,5), including maternal age, parity, prepregnancy weight, history of adverse pregnancy outcomes, low social class, and cigarette smoking.

Recent investigations on adverse pregnancy outcomes have paid special attention to occupational risk factors because a growing number of women work outside their homes and there is a concomitant sharp increase in the number of women who work during their pregnancies. Those risk factors examined include employment in certain industries (6,7); maternal physical effort and posture (8) and prolonged standing (9); exposure to polychlorinated biphenyls (PCBs) (10), noise (11), lead (12), and anesthesia gas (13); shift work (14,15); and job stress (16).

A large body of literature has documented both acute and chronic adverse health

effects of air pollution. The health end points include mortality (17–19), respiratory symptoms (20,21), pulmonary function (22,23), physician office visits (24), and emergency room visits (25,26). However, air pollution is not usually considered a possible determinant of pregnancy outcomes. Recently, an ecological study in the Czech Republic (27) reported an association between infant mortality and total suspended particulates (TSP), and, to a lesser degree, sulfur dioxide (SO₂). A cross-sectional study in China (7) found that the use of coal stoves for heating was significantly associated with low birth weight or preterm birth. Although the data cannot be used to either support or refute a causal inference between air pollution and adverse pregnancy outcomes, it did bring forward some associations that warrant further investigation.

The purpose of this study was to examine the timing and intensity of exposure to TSP and SO₂ during pregnancy and its association with birth weight in a well-characterized cohort, with control for confounding variables. From 1988 to 1991, all pregnant women living in the Dongcheng, Xicheng, Congwen, and Xuanwu areas of Beijing were registered in their local maternal health care center and followed from

early pregnancy until delivery. Individual information on both mothers and infants was collected. Daily air pollution data were obtained independently. The analyses borrowed the strength of the time-series approach while offsetting major limitations in many previous time-series studies, i.e., lack of individual information and reliable denominators from which the cases were derived.

Methods

Study area. Dongcheng, Xicheng, Congwen, and Xuanwu are four adjacent residential areas in the center of Beijing (Fig. 1), covering an area of 45 km². The total population in 1988 was 2,410,360 (641,853 in Dongcheng, 769,900 in Xicheng, 427,449 in Congwen, and 571,158 in Xuanwu), with 1,223,164 males and 1,187,196 females, constituting approximately 35% of the urban population of Beijing. Sociodemographic characteristics, lifestyle, and housing conditions are compatible among the four areas. There are no major industries, and bicycles are the primary form of transportation. Coal stoves, used for heating or cooking in 97% of households, are the major source of air pollution in the areas (23). The residential populations are very stable.

Subjects. The study cohort consisted of all pregnant women who resided in the four areas and delivered live births from 1988 to 1991. In an effort to improve perinatal outcomes, a perinatal health care system was established, under which all resident pregnant women were required to register at their local maternal health care center within 3 months of becoming pregnant. Each

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Maternal Exposure to Neighborhood Carbon Monoxide and Risk of Low Infant Birth Weight

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THE DELETERIOUS EFFECTS of maternal smoking on infant birth weight have given rise to the theory that maternal exposure to carbon monoxide (CO) during pregnancy may increase the risk of delivering a low birth weight infant (1-3). The possibility that CO air pollution, in particular, adversely affects infant birth weight has caused significant concern among residents of Denver, CO (4), who are exposed to the highest levels of residential carbon monoxide in the United States. The annual "Better Air Campaign" has urged Denverites not to drive by publicizing the risk of fetal damage attributable to maternal CO exposure.

There is, however, little epidemiologic evidence regarding the effects of CO air pollution on birth weight. A report of a previous study concluded that mothers residing in Los Angeles residential areas with high levels of air pollution delivered infants of substantially lower birth weight than mothers residing in areas with low levels of total air pollution (5). A complete analysis of the effects of CO air pollution alone was not presented, however.

Further investigation of the effects of CO air pollution on infant birth weight is required to

Synopsis

This case-control study investigated the potential association between ambient levels of carbon monoxide in a pregnant woman's neighborhood of residence and her chance of delivering a low birth weight infant. Low birth weight infants and normal birth weight infants were contrasted with respect to ambient levels of CO during the 3 months prior to delivery in the neighborhoods where their mothers lived at birth.

After adjustment for the confounding effects of maternal race and education, there was no association between higher CO exposure and higher odds of low birth weight. These data do not support a strong association between maternal exposure to neighborhood CO during pregnancy and odds of delivering a low birth weight infant. Further investigation of the effects of CO exposure on birth weight, with direct measurement of total CO exposure, is needed.

direct policy decisions regarding acceptable ambient levels of CO. This retrospective case-control study examined the relation between low birth weight and individual maternal exposure to neighborhood CO during the last 3 months of gestation.

Methods

Air pollution monitoring data of the Colorado Department of Health were used to calculate individual CO exposure for each mother. CO exposure was defined in this study as the time-weighted geometric mean ambient CO level in the mother's neighborhood of residence during the last 3 months of gestation. The selection of the last 3 months of gestation was based on the assumption that the adverse effects of smoking, and thus the potential adverse effects of CO air pollution, are mediated by chronic hypoxia during the last trimester of gestation (6,7).

Low birth weight and normal birth weight infants were identified through birth certificates obtained from the Colorado Department of Health. In order to obtain the most accurate data on maternal CO exposure, the study was restricted



Association of Very Low Birth Weight with Exposures to Environmental Sulfur Dioxide and Total Suspended Particulates

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This paper presents results of a population-based case-control study of the association between maternal exposures to environmental sulfur dioxide and total suspended particulates (TSP) and risk for having a very low birth weight (VLBW) baby, i.e., one weighing less than 1,500 g at birth. The study, which took place between April 1, 1986 and March 30, 1988, comprised 143 mothers of VLBW babies and 202 mothers of babies weighing 2,500 g or more living in Georgia Health Care District 9. Environmental exposure estimates ($\mu\text{g}/\text{m}^3$) were obtained through environmental transport modeling that allowed us to assign environmental sulfur dioxide and TSP exposure estimates at the birth home of each study subject. Exposures less than or equal to $9.94 \mu\text{g}/\text{m}^3$, the median of TSP and sulfur dioxide exposures for the controls, were considered as referent exposures. Exposures to atmospheric TSP and sulfur dioxide above the 95th percentile ($56.75 \mu\text{g}/\text{m}^3$) yielded an adjusted odds ratio of 2.88 (95% confidence interval (CI): 1.16, 7.13), that from above the 75th to the 95th percentile (25.18 – $56.75 \mu\text{g}/\text{m}^3$) yielded an adjusted odds ratio of 1.27 (95% CI: 0.68, 2.37), and that from above the median ($9.94 \mu\text{g}/\text{m}^3$) to the 75th percentile, an adjusted odds ratio of 0.99 (95% CI: 0.51, 1.72). The trend demonstrated in these adjusted estimates suggests an association between VLBW and maternal exposures to high levels of air pollution. *Am J Epidemiol* 2000;151:602–13.

air pollution; environmental exposure; infant, very low birth weight; sulfur dioxide

Very low birth weight (VLBW) babies, most of whom are preterm, weigh less than 1,500 g at birth and account for approximately 1.2 percent of all livebirths (1). The causes of preterm births include premature labor, premature rupture of membranes, and medical induction. The causes of premature labor have not been elucidated (2).

Medically induced, preterm births usually occur because of maternal or fetal complications. Clinical observations suggest that some preterm babies are also small for gestational age (3). Women who have

preeclampsia during pregnancy have a substantially greater risk of delivering VLBW and moderately low birth weight infants and of having preterm and moderately preterm deliveries than do women without hypertension (4).

Factors with well-established links to fetal growth include the infant's sex and racial/ethnic origin; paternal weight and height; and maternal height, prepregnancy weight, gestational weight gain, birth weight, parity, history of a prior low birth weight infant, caloric intake, malaria, cigarette smoking, alcohol consumption, and tobacco chewing (2, 5, 6).

Maternal lifestyle behaviors, such as smoking cigarettes, gaining weight during pregnancy, and using alcohol and recreational drugs play an important role in determining fetal growth. The relation between these lifestyle risk factors and low birth weight is complex and is affected by psychosocial, economic, and biological factors (7–10). Maternal cigarette smoking, the leading known environmental risk factor for low birth weight babies, is also associated with small-for-gestational age babies. In addition, maternal exposure to paternal sidestream smoke or other sources of passive smoke may adversely influence pregnancy outcome (11, 12).

The health effects of living near waste disposal sites or downwind from airborne industrial release sources

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Abbreviations: CI, confidence interval; GHCD9, Georgia Health Care District 9; TSP, total suspended particulates; TSPSO₂, sum of total suspended particulates and sulfur dioxide; VLBW, very low birth weight.

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**SUBJECT: Comments to the Final EIS/EIR for the North Baja Pipeline Project
SCH No. 2001011020 (January 2002)**

Dear Sirs:

The County of Imperial on January 7, 2002, received the Final Environmental Impact Statement/Environmental Impact Report (FEIS/EIR) for the Federal Energy Regulatory Commission (FERC), Bureau of Land Management, Bureau of Reclamation, and State Lands Commission natural gas pipeline project that traverses through Imperial County, for some 60 miles. We have submitted previous correspondence to both federal and state agencies, dated January 9, 2001, February 7, 2001, and September 12, 2001, regarding the proposed PG&E construction and operation of the North Baja Pipeline (NBP) natural gas pipeline from Ehrenberg, Arizona, through Imperial County with a proposed tie-in with Sempra Energy International (SEMPRA) at the Mexican Border.

On Wednesday, January 16, 2002, we understand that the FERC took action on the NBP project and certified the Final EIS/EIR's "Proposed Action" and that the Commission found that the project was in the public's interest and issued an Order ("Certificate of Public Convenience and Necessity") for the proposed pipeline project through Imperial County.

The FERC appears to have acted without due notice or due process, and without consideration of the Imperial County Board of Supervisors concerns as filed both electronically and by hard copy. Copies of comments to FERC are attached. Furthermore we have yet to see how the FERC or CSLC can legitimately make the finding of public need and necessity, particularly when there are alternate sources of "renewable energy" sources that could provide similar amounts of energy and yet not create any of the pollution nor require the extensive gas lines or power lines.